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Catalytic Vapor-Phase Oxidation of—

NICOTINE to NICOTINONITRILE

Nicotinonitrile has been prepared in a maximum yield of 51.5% of theoretical by the vapor-phase air oxidation of nicotine over vanadium pentoxide. Since nicotinonitrile may be readily hydrolyzed to nicotinic acid or nicotinamide in excellent yields, a new process has been made available for niacin or niacinamide.

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PREVIOUSLY reported methods for the oxidation of nicotine to nicotinic acid have been liquid-phase procedures involving the use of excess oxidizing agent. This partial oxidation has been accomplished with a variety of oxidizing agents, such as chromic acid or potassium dichromate (*2*), potassium permanganate (*5*), nitric acid (*8*), and sulfuric acid (*10*). The electrolytic oxidation of nicotine has also produced nicotinic acid in low yields (*11*).

The present investigation was undertaken because of the obvious disadvantages of liquid-phase operation and because vapor-phase oxidation had not been reported heretofore. Early in this study, however, we became convinced that nicotinic acid was not produced in appreciable quantities under any of the conditions imposed, since none could be identified in the reaction products. Nicotinonitrile, however, was found; in fact, a smoke was always one of the reaction products, and this was precipitable in an electrostatic field and identifiable as the nitrile. This oxidative cleavage appears to be unique in the chemistry of nicotine. Although the exact reaction mechanism is not known, the process is considered to be essentially one of oxidation, since water and carbon dioxide are also products of the reaction.

In general, the technique employed approximated that used in the vapor-phase oxidation of benzene (*9*), toluene (*7*), and naphthalene (*1*). Since vanadium pentoxide appeared to be the most suitable catalyst on the basis of a preliminary survey, it was employed in most of the experiments. Other experimental factors, such as reaction temperature, space velocity, and air-nicotine ratio, were also studied. The maximum yield of nicotinonitrile obtained was 51.5% of theoretical. The nitrile is readily hydrolyzable to either nicotinic acid (*6*) or nicotinamide (*4*) in excellent yields.

The limits of flammability of nicotine in dry air at atmospheric pressures and temperatures ranging from 100.5° to 139.5° C. were reported by Jones, Scott, and Miller (*3*) to be 0.75% by volume for the lower limit and 4.00% for the upper. These investigators also reported the ignition temperature of nicotine to be 244° C. in air and 235° in oxygen. Although some of the air-nicotine mixtures passed through the limits of flammability during preheating to reaction temperature, no explosive oxidations were experienced in the present investigation. This fact appears to be explainable on the basis of the time lag on ignition observed by Jones, Scott, and Miller.

Judging from the short space of maximum temperature in the catalyst bed, it is believed that the oxidation is of a "flash" nature. The reaction apparently takes place instantaneously, with

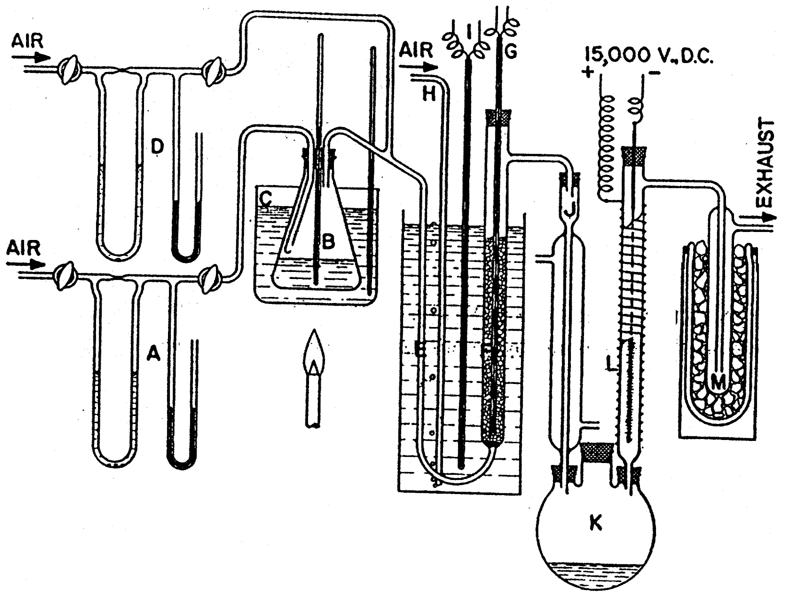

Figure 1. Apparatus for Vapor-Phase Oxidation of Nicotine

period of 3 hours. Distillation of 55.5 grams of residual nicotine (n_D^{20} = 1.5305) yielded 54.7 grams of pure alkaloid (n_D^{20} = 1.5276) and only 0.8 gram of nondistillable tar. Since this quantity of nondistillable material approximated the amount obtained on distilling an equal quantity of the original alkaloid, it was assumed that the questionable error introduced by nicotine oxidation in the vaporizer was negligible.

Although the direct isolation of nicotinonitrile from the reaction products was accomplished in several experiments, it was found more expedient to determine the yield by hydrolyzing the nitrile to nicotinic acid and precipitating the latter as the insoluble cupric salt. The yield of nitrile was calculated from the yield of cupric nicotinate which had been dried to constant weight at 110° C. Yield calculations are reported only on cupric nicotinate samples having a copper content in acceptable agreement with the theoretical value of 20.67%.

This method of evaluating yield appeared justifiable for, as determined by experimental procedures described below: (*a*) The yield of copper nicotinate from a known amount of nicotinonitrile was at least 94.9%; (*b*) comparison of yield values by this method and by direct isolation were in good agreement; and (*c*) examination of the vapor-phase oxidation products revealed no nicotinic acid or products hydrolyzable to nicotinic acid, other than nicotinonitrile. The specific procedure, using the pure nitrile, follows:

complete utilization of nicotine. Some unchanged alkaloid was recovered only in experiment 33, in which the air-nicotine ratio was too low for the formation of nicotinonitrile.

APPARATUS

Figure 1 is a diagram of the apparatus employed. An air-nicotine mixture was obtained by passing a measured quantity of air from flowmeter *A* over the nicotine in vaporizer *B*. This vaporizer was heated in oil bath *C* to the temperature necessary for evolution of the desired quantity of alkaloid. A standard rate of 6 moles of air per hour had been previously employed in establishing the rate of nicotine vaporization at various bath temperatures. This rate of air flow through the vaporizer was employed throughout the runs listed in Table I, and the final air-nicotine mixture was obtained by dilution of the vaporized mixture with an auxiliary air stream from flowmeter *D*. Flowmeters *A* and *D* were calibrated at a pressure of 4 inches of mercury above atmospheric, which was appreciably greater than any back pressure developed in the absorption train.

The gaseous reactants were passed into the U-shaped reactor *E-F*, which was maintained in an electrically heated bath of fused salt. This was continuously stirred by an air stream entering the bottom of the bath through iron tube *H*, and the bath temperature was measured by thermocouple *I*. The reactor consisted of a $^1/_4$-inch iron pipe welded to a $^1/_2$-inch iron pipe. Arm *E* ($^1/_4$-inch inside diameter) served as a preheater for the downward-passing gases prior to their contact with the catalyst in chamber *F* ($^1/_2$-inch inside diameter). The catalyst ranged from 10 to 100 cc., and was generally 6-mesh particle size. The catalyst chamber was fitted with an 18-8 stainless steel well for the chromel-alumel thermocouple, *G*. During operation the thermocouple junction was moved to the maximum exothermic point in the catalyst bed. The exhaust gases from the reactor were conducted, in turn, through a water-cooled condenser, *J*, a 1-liter three-neck receiver, *K*, an electrical precipitator, *L*, and finally through a dry-ice trap, *M*. In preliminary experiments two acid scrubbers were included at the end of this absorption train. Subsequent analysis of the acid solution, however, indicated an absence of products hydrolyzable to nicotinic acid; consequently these scrubbers were eliminated in all experiments here reported.

EXPERIMENTAL PROCEDURE

The nicotine employed had a minimum alkaloid content of 99.0%, and the quantity utilized in each experiment was determined by the loss of weight from vaporizer *B*. In order to establish that the residual nicotine in the vaporizer did not undergo excessive oxidation during the vaporization process, the purity of the unvaporized alkaloid was investigated after a vaporization

A 3.85-gram portion of nicotinonitrile was mixed with a 30 to 1 ratio of constant-boiling hydrochloric acid, and refluxed for 2 hours. Most of the excess hydrochloric acid was removed by distillation, and the concentrate was then evaporated to dryness on the steam bath. The residue was dissolved in approximately 200 cc. of water, adjusted to a pH of 9.2 with 25% sodium hydroxide, boiled with norite, and filtered.

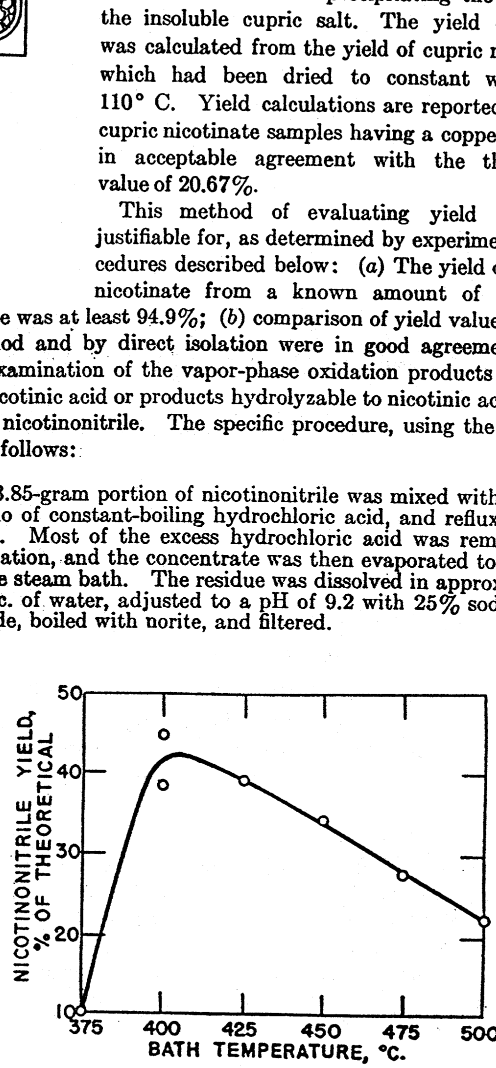

Figure 2. Effect of Bath Temperature on Yields of Nicotinonitrile
(Air-Nicotine Ratio = 150; Space Velocity = 5000)

The clear, cool solution (approximately 225 cc.) was adjusted to a pH of about 2.9 with sulfuric acid. One hundred and fifty per cent of the theoretical amount of cupric acetate, based on a 100% conversion of nicotinonitrile to nicotinic acid, was dissolved in 75 cc. of water. This copper acetate solution was then added to the original nicotinic acid solution, and the mixture allowed to stand for 2 hours. After precipitation of the cupric salt, the pH of the supernatant liquid was 3.9. The pH was lowered to 3.6 by the addition of concentrated sulfuric acid, and the mixture allowed to stand for an additional 30 minutes. The copper nicotinate precipitate was filtered and dried in an oven at 110° C. The 5.4 grams of copper nicotinate obtained represented a 94.9%

TABLE I. EFFECT OF VARIABLES ON YIELD OF NICOTINONITRILE FORMED BY VAPOR-PHASE OXIDATION OF NICOTINE WITH FUSED VANADIUM OXIDE AS CATALYST

Expt. No.	Time of Run, Min.	Temp., ° C. Bath	Temp., ° C. Reactor (max.)	Nicotine Used, Moles	Air Used, Moles	Molar Ratio, Air/Nicotine	Space Velocity	Nicotinonitrile, % of Theory
			Effect of Bath Temperature					
1	180	375	391	0.185	28.1	153	5,010	10.8
2	240	400	457	0.229	37.2	162	5,100	38.6
3	180	400	504	0.202	27.0	133	5,000	44.9
4	180	425	514	0.188	26.0	139	4,990	39.4
5	180	450	547	0.172	25.2	147	5,010	34.4
6	300	475	536	0.273	40.5	148	5,000	28.0
7	300	500	561	0.257	39.2	153	5,005	22.6
			Effect of Space Velocity					
8	150	400	558	0.268	22.5	84	5,020	39.8
9	180	400	508	0.283	27.0	96	5,025	41.1
11	180	400	534	0.316	27.0	86	8,350	46.9
12	180	400	583	0.303	27.0	89	16,750	47.2
13	120	400	534	0.251	21.6	86	30,000	46.3
14	180	400	564	0.278	27.0	97	50,250	34.4
15	120	400	584	0.270	25.2	94	70,500	38.8
16	120	400	499	0.236	25.0	106	7,000	39.7
17	180	400	499	0.214	27.0	126	8,350	44.7
18	150	400	569	0.206	22.5	109	16,750	43.3
19	180	400	518	0.300	32.4	108	30,000	45.3
20	120	400	548	0.321	35.8	112	50,000	46.7
21	210	400	485	0.393	44.1	112	70,200	22.5
22	240	400	482	0.129	21.6	145	3,000	29.8
23	210	400	477	0.178	25.2	142	4,000	36.8
3	180	400	504	0.202	27.0	133	5,000	44.9
2	240	400	457	0.229	37.2	162	5,100	38.6
24	180	400	524	0.226	32.4	143	6,000	42.5
25	135	400	515	0.204	28.4	139	7,010	45.0
26	180	400	467	0.239	37.8	158	7,000	42.6
27	285	400	523	0.372	59.8	161	7,000	40.5[a]
28	180	400	495	0.186	27.0	145	8,350	43.9
29	420	400	421	0.178	25.2	141	10,010	43.0
30	180	400	501	0.225	32.4	144	30,000	42.5
31	150	400	531	0.210	31.5	150	70,000	Trace
			Effect of Air-Nicotine Ratio					
8	150	400	558	0.268	22.5	84	5,020	39.8
9	180	400	508	0.283	27.0	96	5,025	41.1
3	180	400	504	0.202	27.0	133	5,000	44.9
2	240	400	457	0.229	37.2	162	5,100	38.6
10	210	400	412	0.171	32.5	190	5,090	28.7
32	80	450	825	1.230	10.0	8.1	5,000	0.0
33	110	450	588	0.212	15.3	72	5,000	32.2
34	300	450	576	0.427	42.0	98	5,000	32.5
35	150	450	559	0.206	20.8	101	5,000	29.2
36	180	450	557	0.200	24.9	124	4,960	35.4
5	180	450	547	0.172	25.2	147	5,010	34.4
37	240	450	512	0.180	33.5	192	5,000	31.4
38	360	450	525	0.262	50.2	193	4,975	32.7
39	240	450	495	0.153	33.5	219	5,000	33.1
40	360	450	488	0.190	50.4	265	5,000	27.2
16	120	400	499	0.236	25.0	106	6,970	39.7
41	210	400	500	0.380	44.1	116	7,000	25.1
42	150	400	521	0.249	31.5	126	6,910	35.2
26	135	400	515	0.204	28.4	139	7,010	45.0
27	180	400	467	0.239	37.8	158	7,000	42.6
28	285	400	523	0.372	59.8	161	7,000	40.5[a]
43	120	400	468	0.130	25.2	194	6,990	28.0
44	180	400	419	0.172	37.8	220	7,000	26.6
45	150	400	417	0.140	31.5	225	7,000	31.7

[a] Nicotinonitrile yield determined by direct isolation.

yield. Analysis of this copper salt gave 20.87% copper (theoretical 20.67). In view of this yield of copper nicotinate from the pure nitrile by the process employed on the reaction mixtures, it appears that the actual yields of nicotinonitrile are slightly higher than those reported here.

Experiment 27 (Table I) was made for the purpose of identifying the reaction products. The reaction mixture was washed from the receiving system with a mixture of ether and methanol. The odor of hydrogen cyanide was detected in the reaction products, and its presence was confirmed by a positive color reaction of the vapors with a paper moistened with sodium picrate solution. After distillation of the methanol and ether at atmospheric pressure, the residual liquid was fractionated at approximately 12-mm. pressure. The 15.7-gram fraction boiling at 89° C. had a melting point of 48.8–50.8° C. (uncorrected) and showed no depression in melting point when mixed with a known sample of nicotinonitrile. This represented a 40.5% yield of nitrile, which compares favorably with experiment 26, made under similar conditions, where the nitrile was hydrolyzed to nicotinic acid and precipitated as the copper salt, giving a 42.6% yield. No other product hydrolyzable to nicotinic acid was found.

To confirm the fact that the reaction product was mainly nicotinonitrile and not nicotinic acid or another product hydrolyzable to it, the reaction product from 69.2 grams of nicotinic was divided into two equal portions. The experimental conditions were: Space velocity, 5000; ratio of air to nicotine, 98; and bath temperature, 450° C. The first portion was analyzed according to the procedure outlined for hydrolysis of pure nicotinonitrile; the second portion was distilled under diminished pressure to isolate the pure nitrile directly. By the copper salt method a yield of 30.9% nicotinonitrile was indicated. The second portion by direct isolation produced a 41% yield of very crude nicotinonitrile; upon second fractional distillation, a 25.2% yield of pure nicotinonitrile was obtained with a melting point of 49.0–50.7° C. (uncorrected). The yields in this experiment check favorably with those obtained by the copper salt method in experiments 34 and 35 under similar conditions.

Since this investigation was concerned primarily with determination of the optimum conditions for the production of nicotinonitrile, other reaction products were not extensively studied. In spite of our failure to detect traces of nicotinic acid in the oxidation products, there was no conclusive evidence against the formation of minute amounts of the acid. Traces of the acid could possibly be formed by the oxidation of nicotine or by a secondary reaction between water and nicotinonitrile.

TABLE II. EFFECT OF CATALYSTS ON YIELD OF NICOTINONITRILE FORMED BY VAPOR-PHASE OXIDATION OF NICOTINE

Expt. No.	Catalyst	6-Mesh Catalyst Used, Cc.	Time of Run, Min.	Temp., ° C. Bath	Temp., ° C. Reactor (max.)	Nicotine Used, Moles	Air Used, Moles	Molar Ratio, Air/Nicotine	Space Velocity	Nicotinonitrile, % of Theory
46	Porous V_2O_5	100	120	450	...	0.203	16.7	82	5,000	51.5
12	Fused V_2O_5	30	180	400	583	0.303	27.0	89	16,750	47.2
47[a]	V_2O_5 on porous plate	100	120	450	...	0.169	NH_3 1.1, air 15.7	NH_3 + air 101	5,020	34.9
48	V_2O_5 on porous plate	100	120	450	...	0.208	16.7	80	5,000	21.2
49	V_2O_5 on acid-treated kaolin	100	180	450	604	0.166	25.1	151	5,000	26.4
50	V_2O_5 on Al	65	120	450	502	0.153	22.0	144	10,170	23.2
51	V_2O_5:MoO_3(1:1) on acid-treated pumice	100	120	450	567	0.216	16.6	77	5,000	9.3
52	V_2O_5 on activated alumina	30	180	350	784	0.328	27.0	82.4	15,500	7.9
53	V_2O_5 on kaolin	30	180	400	666	0.238	27.0	113	16,700	7.1
54	MoO_3 on porous plate	100	120	500	530	0.117	15.6	134	5,000	6.1
55	Silver vanadate on acid-treated pumice	100	120	450	473	0.131	16.8	128	5,000	Trace
56	V_2O_5 pptd. with *o*-phosphoric acid on porous plate	100	120	450	496	0.199	16.6	83.5	4,990	Trace
57	V_2O_5 on pumice	100	120	450	858	0.260	16.6	64	5,000	Trace
58	CuO on acid-treated pumice	85	120	450	883	0.268	16.6	62	5,880	Trace
59	$KHSO_4$ on acid-treated pumice	100	120	450	468	0.239	16.6	70	5,000	Trace
60	TiO_2 on kaolin	100	120	450	805	0.226	16.6	74	5,000	Trace
61	V_2O_5 on iron	75	120	450	464	0.288	16.6	58	7,330	Trace
62	V_2O_5:ThO_2(3:2)	70	120	450	755	0.248	16.6	67	7,150	Trace
63	Alkali-treated kaolin	100	120	450	835	0.313	16.6	53	5,000	Trace
64	Platinized aerogel, 0.027% Pt[b]	75	120	450	616	0.301	16.6	55	6,680	Trace
65	No catalyst	...	60	450	455	0.128	8.32	65	∞	None

[a] Ammonia used in this experiment. [b] Supplied by D. B. Keyes, University of Illinois.

A fused vanadium oxide catalyst was used with all the experiments listed in Table I; shown graphically in Figures 2, 3, and 4

EFFECT OF VARIABLES

TEMPERATURE. Both the bath temperature and the maximum exothermic temperature are reported for most of the experiments. The exothermic temperature varied somewhat during each run and could not be determined accurately at any given instant because of slight shifts in the position of the maximum exothermic

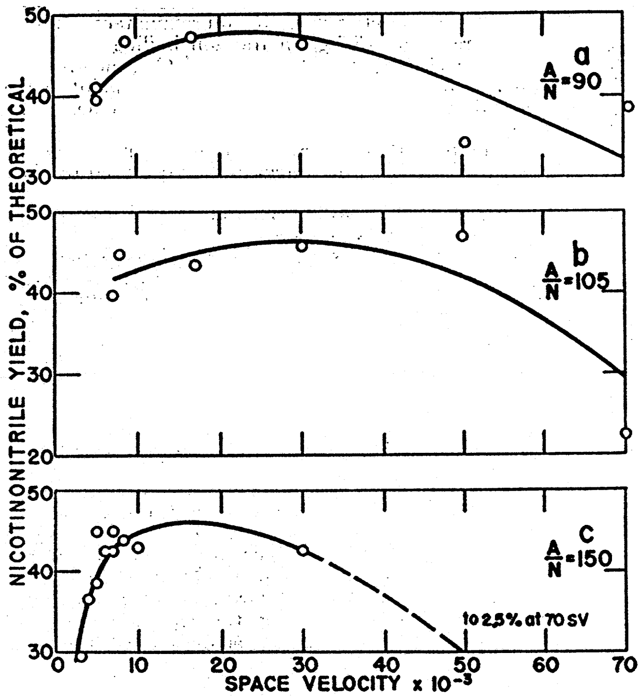

Figure 3. Effect of Space Velocity on Yields of Nicotinonitrile at 400° C. and Indicated Molar Air-Nicotine Ratios A/N

point within the catalyst bed. In view of the fact that bath temperature could be accurately controlled, this value was employed in illustrating the experiments in Figures 2 to 4, although the maximum exothermic temperature is a more accurate value for actual reaction temperature. It should be borne in mind, therefore, that Figures 2 to 4 are representative of data applicable only to an iron reactor of 1/2-inch inside diameter. Figure 2 illustrates experiments 1 to 7 (Table I). With a space velocity of approximately 5000 and a molar air-nicotine ratio of about 150, the optimum bath temperature was 400° C. Comparison of *a* and *b* (Figure 4) reveals that a temperature of 400° C. was more productive than 450° for the molar air-nicotine ratios of 100 and 150.

MOLAR AIR-NICOTINE RATIO. The effects of various air nicotine ratios upon the yields of nicotinonitrile are graphically expressed in Figure 4. When the space velocity was 5000 and the bath temperature 400° C. (4*a*) the optimum molar air-nicotine ratio was about 135. With a space velocity of 5000 and bath temperature of 450° C. (*b*) and a space velocity of 7000 and bath temperature of 400° C. (*c*), the optimum molar air-nicotine ratios were about 150 and 160, respectively. It would appear, therefore, that within space velocity limits of 5000 to 7000 and at bath temperatures of 400° and 450° C. the optimum range of air-nicotine ratios is approximately 135 to 160.

SPACE VELOCITY. In this paper space velocity is defined as the ratio of liters of gases at reaction temperature per hour to liters of catalyst employed. The influence of space-velocity variations on the yields of nicotinonitrile (experiments 8 to 31, Table I) are graphically represented in Figure 3. At a bath temperature of 400° C. and with molar air-nicotine ratios of about 90 and 105, the optimum space velocity range was about 9000 to 50,000. With a molar air-nicotine ratio of 150 and a bath temperature of 400° C. the variation from optimum yield was not appreciable within the space velocity range of 6000 to 30,000.

Experiments 15, 21, and 31 (temperature 400° C., space velocity about 70,000) indicate that the yields of nicotinonitrile are inversely proportional to the air-nicotine ratio. It is obvious that this series should be extended in the direction of lower ratios. Since the present equipment, however, is not well adapted for the relatively high input of nicotine at such high space velocities, this point will be further studied with modified apparatus.

EFFECTIVE CATALYSTS

Table II discloses the effectiveness of various catalytic agents studied. The experiments on catalysts other than fused vanadium pentoxide are only of qualitative value, in that they indicate a catalytic effect which has not been extensively studied. These data do not demonstrate the relative effectiveness of the catalysts listed, since the optimum conditions for each catalyst were not determined. It may be concluded, however, that the materials listed have some catalytic effect on the oxidation of nicotine to nicotinonitrile, since no nitrile was obtained in the absence of a catalyst.

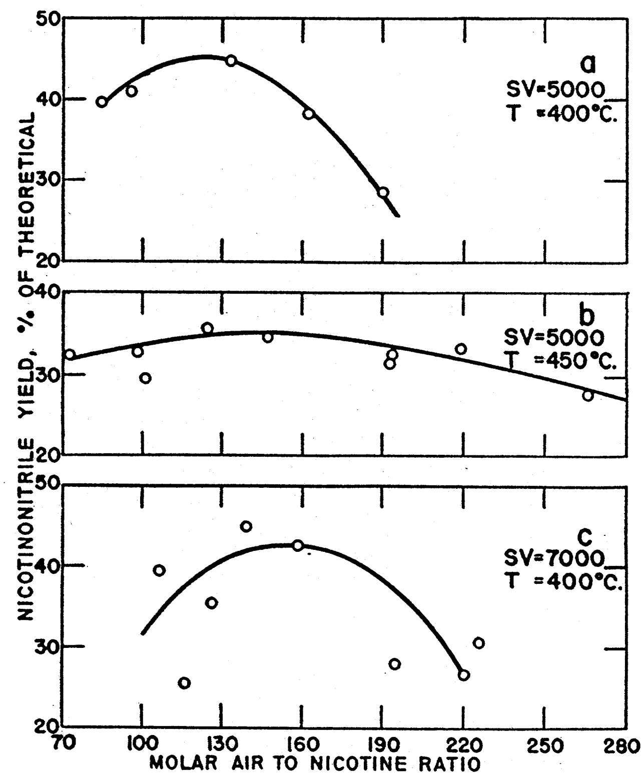

Figure 4. Effect of Molar Air-Nicotine Ratios on Yields of Nicotinonitrile at Indicated Bath Temperatures T and Space Velocities SV

The highest yield of nicotinonitrile (51.5%) was obtained in experiment 46 with a porous vanadium pentoxide catalyst. This catalytic material was prepared by the addition of an excess acetic acid to a hot aqueous solution of ammonium vanadate. The precipitated vanadium oxide was filtered and dried at 150° C. Although this catalyst appeared to be somewhat more effective than fused vanadium oxide, it did not possess the necessary rigidity for continued use.

Porous plate, acid-washed kaolin, activated alumina, pumice, aluminum, and iron were employed as carriers for vanadium pentoxide with some success. Molybdenum oxide on porous plate and vanadium pentoxide–molybdenum oxide (1 to 1) mixture on acid-treated pumice had some catalytic action. Traces of nitrile were detected when the following were employed as catalysts: silver vanadate on acid-washed porous plate, vanadium pentoxide on iron, platinized aerogel, alkali-washed kaolin, vanadium pentoxide–thorium oxide (3 to 2), titanium dioxide on kaolin, and cupric oxide or potassium bisulfate on acid-washed pumice.

The activity of the fused vanadium pentoxide was retained over an extended period of use. In experiment 38 a 31.7% yield of nitrile was obtained after the catalyst had been used for 13 hours. After 97 hours a 33.1% yield of nicotinonitrile was obtained in experiment 39 under experimental conditions otherwise comparable to those of experiment 38.

ACKNOWLEDGMENT

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